REMARKS

Claims 1-8, 14-20, 53 and 59-60 are pending. Claims 15, 19-20 and 53 were previously withdrawn from examination.

Claim Rejections under 35 U.S.C. § 103

Rejection over Quakyi et al. in view of Jennings et al., in light of Wakarchuk et al.

Claims 1-3 were rejected under 35 U.S.C. 103(a) as being unpatentable over Quakyi *et al.* (Infect. Immun. 65(5):1972-1979) in view of Jennings *et al.* (Molecular Microb. 18(4):729-740), in light of Wakarchuk *et al.* (J. Biol. Chem. 271(32):19166-19173). Applicants respectfully traverse this rejection.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness for Claims 1-3 over Quakyi *et al.* in view of Jennings *et al.* and in light of Wakarchuk *et al.*.

The Examiner has erred in her characterization of the teachings Quakyi *et al.*, Jennings *et al.* and Wakarachuk *et al.*.

Quakyi *et al.* examined the toxicity of (i) purified LOS from 3 different meningococcal strains (encapsulated group B strain M986 (serotype 2a), noncapsulated strain M986-NCV-1 (serotype 2a), and a truncated M986 LOS mutant strain OP$^-$), (ii) LOS in OMVs from each strain and (iii) LOS in D-OMVs from each strain. See pages 1972-1973. The toxicity of LOS examined by Quakyi *et al. i*s associated with the Lipid A component of LOS. See page 1972, second column, first full paragraph; and page 1978, final paragraph. Applicants' representative is not aware of any teaching of a lgtB 03 strain in Quakyi *et al.* as suggested by the Examiner on page 3, second full paragraph, of the Office Action.

Jennings *et al.* presented the identification and isolation of a locus from *Neisseria meningitidis* (Nm) by homology with a hybridization probe from the *Haemophilus influezae lic2A* gene. See page 730, first column first full paragraph. To confirm the role of these genes in LPS biosynthesis, they transformed an L3 immunotype derivative of strain MC58, to inactive the genes individually and also in combinations. See page 733, Mutagenesis of the lgtABE locus, for example, first paragraph under this heading.

Jennings *et al.* suggest that the combined data from the immunological and T-SDS-PAGE analysis of LPS from the mutants suggest that the *lgt* locus genes encode the glycosyl transferases for the biosynthesis of lacto-N-tetraose and that *lgtB* gene encodes the transferase catalyzing the β1-4 linkage of the terminal galactose to N-acetylglucosamine. See page 734, left column, first full paragraph. Jennings *et al.* do not discuss blebs, nor that "blebs having truncated LOS are less toxic," as suggested by the Examiner on page 3 of the Office Action, third full paragraph. However, the absence of a discussion of toxicity is not surprising. The safety issue raised by the saccharide component of LPS is distinct from the toxicity associated with the Lipid A portion of LPS. Studies of the saccharide component of LPS affected by the mutants discussed by Jennings *et al.* have demonstrated the heterogeneity of LPS. This heterogeneity has been used to divide the strain into 12 immunotypes. The presence of galactose-containing structures, such as Galα(1-4)βGal and lacto-*N*-tetraose, could lead to immunopathology due to cross-reactivity with similar human structures. See page 737, first column, final paragraph – second column, first paragraph. The safety issue raised by this saccharide component of LPS is distinct from the toxicity associated with the Lipid A portion of LPS described by Quakyi et al. Therefore, Jennings *et al.* examined issues of safety associated with the saccharide component of LPS while Quakyi *et al.* studied the toxicity associated with a different component of LPS, the lipid A portion of LPS.

Wakarchuk *et al.* also studied the saccharide component of LPS. Specifically, they examined the functional relationships of the genetic locus encoding the glycosyltransfease enzymes involved in expression of the lacto-*N*-neotetraose terminal saccharide structure in *Neisseria meningitidis*. As discussed above the saccharide component of LPS is distinct from the Lipid A component of LPS. Futhermore, the *N. meningitidis* immunotype L3 strain from which the mutants were generated by Wakarchuk *et al.* is not the same strain as taught by Quakyi *et al.*, as suggested on page 3 of the Office Action.

In summary, Applicants' representative is not aware of any teaching of a lgtB 03 strain in Quakyi *et al.* Jennings *et al.* do not discuss blebs, nor that "blebs having truncated LOS are less toxic." Jennings *et al.* examined issues of safety associated with the saccharide component of LPS while Quakyi *et al.* studied the toxicity

associated with a different component of LPS, the lipid A portion of LPS. The *N. meningitidis* immunotype L3 strain from which the mutants were generated by Wakarchuk *et al.* is not the same strain as taught by Quakyi *et al.*

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness for at least the reasoning that the Examiner has failed to establish a rational underpinning to support a legal conclusion of obviousness based on the Graham factors. Furthermore, the cited art does not teach each and every element of Applicant's claimed invention. Applicants request that this this rejection be withdrawn.

Rejection over Quakyi et al. in view of Jennings et al., in light of Wakarchuk et al., and further in view of Berthet et al. and Gu et al.

Claims 4-8, 14-18, 59 and 60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quakyi *et al.* (Infect. Immun. 65(5):1972-9), in view of Jennings *et al.* (Molecular Microb. 18(4):729-740), in light of Wakarchuk *et al.* (J. Biol. Chem. 271(32):19166-19173), as applied to claims 1-3 above, and further in view of Berthet *et al.* (WO 01/09350) and Gu *et al.* (Infect. Immun. 61(5):1873-1880). Applicants respectfully traverse this rejection.

The shortcomings of Quakyi *et al.*, Jennings *et al.* and Wakarchuk *et al.* are discussed above. The mischaracterizations of Berthet *et al.* and Gu *et al.* are set forth below.

First, Berthet *et al.* do not exemplify a *N. meningitidis* B strain as taught by Quakyi et al, as suggested on page 4 of the Office Action. The strains discussed by Quakyi *et al.* retained varying concentrations of lipooligosaccharide (LOS). In contrast Berthet *et al.* describe a strain that lacks capsular polysaccharide, for example, page 42 of Berthet *et al.* cited by the Examiner.

Furthermore, the Examiner's characterization of column 7, lines 42-43, of Gu *et al.* (Infect. Immun. 61(5):1873-1880) on page 5 of the Office Action is inaccurate. The Examiner suggests that in column 7, lines 43-43, Gu *et al.* specifically teach that the predominant LOS type in the group B disease strains is L3. In contrast, column 7 on page 1876 relates to chemical characterization of AH-OS and OS-TT conjugates. Gu *et al.* use group A strain A1 LOS as a vaccine candidate. See Materials and

Methods. Further characterizations of Columns 1 and 2 are also unclear. The reference to Column 4 page 60-65 in Gu *et al.* is unclear.

Applicants respectfully submit that the Examiner has failed to establish a *prima facie* case of obviousness for at least the reasoning that the Examiner has failed to establish a rational underpinning to support a legal conclusion of obviousness based on the Graham factors.

Applicants respectfully submit that pending claims 4-8, 14-18, 59 and 60 are patentable over Quakyi *et al.*, in view of Jennings *et al.*, in light of Wakarchuk *et al.*, as applied to claims 1-3 above, and further in view of Berthet *et al.* and Gu *et al.*, and respectfully request that this rejection be withdrawn.

CONCLUSION

Should any outstanding issues remain, the Examiner is encouraged to contact Applicants' undersigned representative.

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